

104,526981

PCT/GB03/3853

The Patent Office  
Concept House  
Cardiff Road  
Newport  
South Wales  
NP10 8QQ

07 MAR 2005

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.



**PRIORITY  
DOCUMENT**  
SUBMITTED OR TRANSMITTED IN  
COMPLIANCE WITH RULE 17.1(a) OR (b)

Signed *AmB...*

Dated 26 September 2003

Best Available Copy

# Patents Form 1/77

Patents Act 1977  
(Rule 16)

The  
Patent  
Office

13JUN03 EB14697-1 D10007  
P01/7700 0.00-0313657.9

THE PATENT OFFICE

12 JUN 2003

LONDON

## Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

13 JUN 2003

The Patent Office

Cardiff Road  
Newport  
South Wales  
NP9 1RH

1. Your reference

NEWPORT

P3118a GB PRO

2. Patent application number

(The Patent Office will fill in this part)

0313657.9

3. Full name, address and postcode of the or of each applicant (underline all surnames)

EPIGEM LIMITED  
MALMO COURT  
KIRKLEATHAM BUSINESS PARK  
REDCAR TS10 5SQ

Patents ADP number (if you know it)

7021991003

If the applicant is a corporate body, give the country/state of its incorporation

GB

4. Title of the invention

MICROFLUIDIC SYSTEM

5. Name of your agent (if you have one)

NOVAGRAAF PATENTS LIMITED

"Address for service" in the United Kingdom to which all correspondence should be sent (including the postcode)

THE CRESCENT  
54 BLOSSOM STREET  
YORK YO14 1AP

Patents ADP number (if you know it)

08299166001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number

Country

Priority application number  
(if you know it)

Date of filing  
(day / month / year)

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application

Date of filing  
(day / month / year)

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? (Answer 'Yes' if:

- a) any applicant named in part 3 is not an inventor, or
  - b) there is an inventor who is not named as an applicant, or
  - c) any named applicant is a corporate body.
- See note (d))

YES

**Patents Form 1/77**

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form

Description

18

Claim(s)

Abstract

Drawing(s)

12

10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (Patents Form 7/77)

Request for preliminary examination and search (Patents Form 9/77)

Request for substantive examination (Patents Form 10/77)

Any other documents (please specify)

11.

I/We request the grant of a patent on the basis of this application.

Signature

Date

NOVAGRAAF PATENTS LIMITED

12/06/2003

12. Name and daytime telephone number of person to contact in the United Kingdom

PETER WILSON (DR)

01904 610586

**Warning**

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

**Notes**

- If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505.
- Write your answers in capital letters using black ink or you may type them.
- If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.
- If you have answered 'Yes' Patents Form 7/77 will need to be filed.
- Once you have filled in the form you must remember to sign and date it.
- For details of the fee and ways to pay please contact the Patent Office.

## MICROFLUIDIC SYSTEM

The invention relates to a microfluidic system having a modular construction for rapid assembly and disassembly.

5

Microfluidic devices and systems have become increasingly important in recent years for performing large numbers of different chemical and/or biological operations on a manageable scale, since they allow a large number of chemical or biochemical reactions to be carried out as part of an analytical and/or synthetic process in a relatively small liquid volume. Such miniaturised analytical or synthetic operations are generally more efficient, producing increased response times and reduce the requirement for potentially expensive reagents.

10

Conventional microfluidic devices and components have been constructed on a chip using technology analogous to that followed in the silicon fabrication industry in general, for example by constructing the devices in a planar fashion using photolithography and etching techniques. Conventionally, there has been a tendency, in particular by analogy with miniaturisation elsewhere in the silicon industry, to concentrate development efforts on miniaturising onto a single chip of as small a size as possible all chemical, biochemical and biological processing associated with a particular synthetic and/or analytical process.

20

Such constructions offer many advantages. However, the resultant chip is relatively inflexible. It is not always easy to intermix different materials and device technologies within such a single chip. Inspection, maintenance and repair can be complex.

25

It is an object of the invention to provide a microfluidic system which offers enhanced flexibility and which mitigates some or all of the disadvantages of single chip integral systems.

- 5 It is a particular object of the present invention to provide a modular microfluidic system in which various different microfluidic components are readily assemblable and disassemblable into a complete system to offer enhanced flexibility and utility.
- 10 Thus, according to the present invention in its in a first broadest embodiment there is provided a modular microfluidic system comprising at least one base board having a plurality of fluidly linked fluid supply apertures, preferably further having at least one fluid source aperture fluidly linked thereto, a plurality of microfluidic modules adapted to be detachably attached to the base
- 15 board, each having one or more fluid inlets and/or outlets, and a plurality of fluid couplings to effect releasable fluid connection between a module and a base board via a supply aperture on the base board and an inlet/outlet on the module.
- 20 In accordance with the invention, the microfluidic circuit is built up on the base board, with the "laboratory" system being formed in modular fashion upon the base board chip, rather than being integrated therewith in conventional manner. Fluid is supplied to the constructed microfluidic system via the fluid source aperture in the baseboard or by direct introduction into a
- 25 module. The base board chip is preferably constructed to provide a plurality of fluid channels and/or chambers linking in fluid communication at least some of the supply apertures to each other and/or to the source aperture. The fluid supply passages within the modules complete a desired microfluidic circuit when the modular structure is assembled.

The invention offers significant advantages, particularly in relation to flexibility of construction in use, when compared with prior art systems. Chip module to base board interconnections may be made conveniently compact and simple, whilst at the same time connections between the board and external equipment can utilise well established fittings for interfacing to that equipment. Intermixing of different materials and device technology is enabled (for example glass chips on a polymer board). In the same way a choice of external systems such as external pumps against on-board or module-surface mounted pumps and valves etc. is offered.

The system of the invention offers flexibility of design choice. For example a simple baseboard design may be provided with exchangeable complex modules, or complex systems may be included within the baseboard, with the modules attachable thereto being simple and/or disposable. Seals and connections between module and board can be selected according to module function.

The overall system provides for simple inspection and maintenance, flexibility of use, and ease of repair to systems, for example by replacing only a module which is defective rather than an entire system.

A microfluidic module in accordance with the invention comprises one or more microfluidic devices. As used herein, a microfluidic device may comprise any known element of a microfluidic system, including without limitation an active device unit, such as a reactor, heater, cooler, analyser, detector, mixer, processor or the like, a fluid function unit such as a pump, valve, filter or the like or merely a fluid channel and/or chamber to complete a particular microfluidic circuit.

Microfluidic devices in accordance with the invention may be three dimensional or generally planar. In a preferred embodiment, the devices are generally planar. Each module has a generally planar construction to be  
5 incorporated upon a generally planar baseboard. Inlet/outlet apertures are most conveniently provided on one of the planar faces of such a module. Supply apertures are most conveniently provided on a planar face of the baseboard, and source aperture(s) may be provided at an edge or the same or opposite planar face thereof.

10

In particular, each module preferably has a generally planar sandwich construction, comprising at least one inner sandwich layer defining a fluid channel and/or chamber portion, and at least one cover layer covering and effecting enclosure of the same. In a preferred embodiment the module  
15 comprises at least one sandwich layer defining an enclosed fluid channel and/or chamber portion, for example consisting of paired sandwich elements into the surface of at least one of which channels are created such that the pair assembled together define such an enclosure, with cover layers at either side thereof. Further intermediate layers may be present.

20

Active microfluidic elements may be incorporated within the channels and/or chambers so formed in the sandwich layer or additionally or alternatively may be provided upon the module surface in fluid communication with the channel therewithin. One or more inlet and/or outlet apertures are provided to effect a  
25 fluid communication between the channel and an external surface of the module, for fluid connection to the baseboard. A baseboard may be similarly constructed.

Sandwich layers and cover layers are conveniently fabricated in suitable plastics material. Sandwich layers, which contact fluid in use, are preferably fabricated from chemically resistant plastics material, such as epoxy, SU8 epoxy being most preferred. This gives good resistance with good fabricability of fluid channels and chambers. Cover layers including fluid inlet/outlet ports might also contact fluid in use, and accordingly these are also preferably fabricated from materials exhibiting good chemical resistance, for example epoxy or other plastics such as polyetheretherketone (PEEK).

Chemical properties of merely structural cover or intermediate layers might be less critical. However, any layers and in particular cover layers might also be modified for specific properties, for example for transparency, for electrical, magnetic or dielectric properties, to provide mountings for externally mounted microfluidic device components etc.

15

In practice, different parts of individual components might have different functional requirements, for example regarding transparency, structural strength, chemical resistance etc. Combinations of materials may be used, for example using a combination of materials and components and by using composite substrates for the baseboard and chips to achieve the best combination of properties.

20

For example, in the case of a microchemical reactor it is beneficial to use a substrate polymer that is transparent to enable easy inspection of the fluid path. It will be understood however that a readily available polymer with good transparency that is also resistant to a wide range of solvents used in synthetic chemistry is not generally available. By adopting a composite approach a substrate can be readily formed comprising a basic structure of transparent material (not necessarily exhibiting high chemical resistance) but in which

25



inserts of chemically resistant material (not necessarily exhibiting high transparency) are included in the substrate in regions where solvent contact is possible; preventing contact with the less resistant "window" substrate material.

5

As used herein, microfluidic will be understood to refer to microstructures having at least some sub-millimetre dimensions, microstructure in this case being used to refer to any of a variety of well known structures in such systems, including, but not limited to, the channels and chambers hereinabove  
10 described, that are capable of providing passage or storage for a fluid.

In accordance with the invention, a plurality of fluid couplings are provided to effect a fluid-tight connection between at least one fluid supply aperture on a base board and at least one inlet/outlet on a microfluidic device module.

15 Conveniently, this connection comprises a releasable coupling, for example in the form of a channel means removably insertable into a suitable recess in such a inlet/outlet/aperture to effect a fluid tight communicating connection therebetween. Such channel means conveniently comprises a tubular element, in particular a rigid tubular element, for example being parallel sided, for  
20 example being square or rectangular, polygonal, or alternatively having a circular or elliptical cross section, with any recess into which such a tubular element is to be received preferably being shaped accordingly.

Such a tubular element can be a separable and distinct unit. However, for  
25 convenience, particularly in relation to the preferred embodiment where base board and module comprise generally planar components, the tubular element preferably comprises a projecting ferrule integral with and projecting from a first aperture comprising either a fluid supply aperture in the base board or an inlet/outlet in the module, and adapted to be received in a recess comprised as

a second aperture, correspondingly either an inlet/outlet in the module or a supply aperture in the base board. In particular the ferrule projects generally perpendicularly from a generally planar surface, to effect a fluid connection between a base board and module adapted to lie generally parallel when connected.

In a most preferred form, ferrules are provided which project above the surface of the base board to be received within recesses comprising the inlet/outlet apertures of modules to be attached thereto.

10

Ferrules as above described can offer particular advantages. The ferrule system enables dead volume in fluid path between "chips" to be minimised. Use of ferrules allows higher density of interconnections than other fittings such as HPLC fittings and the like. Ferrules can withstand high pressures.

15 Ferrules generally require a reduced thickness of material in which to be held compared to the thickness needed to hold a screw thread or like fitting, allowing much thinner layers, down to layers essentially comprising films, to be interconnected. One or a few mechanical fasteners can be used to hold together a system making multiple fluid connections through the ferrules.

20

The ferrules ensure accurate mechanical alignment of fluid elements making accurate module placement easy.

It is generally easy to machine suitable ferrule recesses within the materials typically envisaged for use for baseboard and modules, giving scope for a range of ferrule and recess shapes. The internal bore and external diameter can be varied within limits, making it possible for the ferrule to incorporate microfluidic functionality. For example the internal bore could incorporate a filtration function, optionally comprising multiple holes (in manner analogous

25

to a photonic crystal). For example the ferrule can be modified to a larger shape to include a reservoir function.

5 Optionally the ferrule can incorporate additional functionality. It may contain a non-return valve, for example a ball valve. The ball valve could conveniently be magnetically switchable valve. The ferrule could contain a catalyst frit or could incorporate a filter. Various switches could be conceived.

10 It is possible to use a conducting for example metallic ferrule for electrical interconnection between chips. Such a metallic ferrule may optionally be provided with an insulating layer on a fluid and/or module contacting surface, effecting an electrical contact between modules and/or electrical contact with fluid therein. A ferrule based design offers particular flexibility in that the system may readily be provided with further functional interconnections (eg  
15 magnetic, optical) either integral with or separately from the ferrule.

Optionally the ferrule can incorporate or be provided with a closure for closing a pathway not being used in a particular device combination allowing redundancy in pathway choice in base board for example during plug and play  
20 use. The closure may comprise a bung to be applied by a user, or an integral closure valve adapted to be operated manually, or to operate automatically on insertion of ferrule into recess.

The invention hereinabove has been described in terms of a single baseboard with a plurality of modules disposed in a single layer thereupon. It will be  
25 readily appreciated that the invention is not so limited. A particular flexibility of the invention is that it allows for multi-level stacking of modules and/or base boards and/or intermediate level boards. Such intermediate level boards may serve merely to provide fluid connections in the form of channels,

chambers or the like, or may also include active microfluidic components. Similarly, it will be understood that the invention encompasses modular structures comprising a plurality of modules as hereinbefore described and at least one base board, in which the base board is also optionally provided with active microfluidic components.

Intermediate level boards may be constructed as above described and preferred features thereof will be construed by analogy. In particular, boards are preferably planar, and preferably of a sandwich construction as above.

10

In embodiments comprising such a multi-level stacking system, any component adapted for use at an intermediate level will comprise at least one inlet aperture on a first "lower" surface and at least one outlet aperture on a second "upper" surface (it being understood that lower and upper are being used herein as a convenience to refer to surfaces proximal and distal to the base board, and not to imply any restrictive orientation). References herein to inlets/outlets in a module will be understood to apply equally where appropriate to such a lower aperture, and references herein to a base board fluid supply aperture will be understood to apply equally where appropriate to such an upper aperture in an intermediate level component. It is particularly easy to stack multiple layers using the preferred ferrule embodiment.

20

In a preferred embodiment, fluid connections are effected by projecting ferrules between components adapted to lie generally parallel. In multi-level systems, it will be convenient that these ferrules all project in the same direction. In particular, ferrules are preferably provided at apertures in the upper surface of the base board and at apertures in the upper surface of all intermediate level modules, to be receiving engaged in fluid tight connection

25

within recessed portions at apertures on the lower surface of all intermediate level components and all top level components.

Attachment of a module to the board, or of an upper layer module, to a lower layer module in multi-layer systems, may be achieved by any suitable releasable attachment means, including without limitation screws or screw fixings, bayonet fittings whether quick release or not, push and snap fit connectors, vacuum or mechanical clamping connections, releasable mutually engageable resilient hook and felt pads, hooks, clips etc. The fluid couplings themselves, especially in the preferred form as channel means in interference fit between pairs of linked apertures, for example ferrules engaged in interference fit in recesses, may assist in or even suffice to constitute such mechanical connection. However, additional mechanical connectors will usually be preferred.

15

The system in accordance with the invention provides a plurality of interchangeable elements enabling a plurality of different microfluidic functions to be performed, on one or more levels.

20 The invention will now be described by way of example only with reference to Figures 1 to 8 of the accompanying drawings wherein:

Figure 1 illustrates in cross section how fluid connection is effected between components in accordance with the invention;

Figure 2 is a schematic illustration of a simple basic construction of a microfluidic device for use with the invention;

25

Figure 3 is an example microreactor system employing the principles of the invention;

Figure 4 is a plan view of the baseboard of the reactor of Figure 3;

Figure 5 is an on chip manifold from the reactor of Figure 3;

Figure 6 is a plan view of a first active microfluidic device from the reactor of Figure 3;

Figure 7 is a plan view of a second active microfluidic device from the reactor of Figure 3;

5 Figure 8 is plan view of a third active microfluidic device from the reactor of Figure 3;

Figures 9 and 10 are examples of composite microfluidic device/ substrate arrangements using a combination of materials to achieve the best combination of properties;

10 Figures 11 and 12 are examples of reactor chip arrangements employing the composites of figures 9 and 10.

Figure 1 illustrates in cross section the basic design of fluid connection in accordance with the preferred embodiment of the invention employing  
15 projecting ferrules.

Illustrated schematically in Figure 1 are a baseboard (1), a first level component layer (2) and a second level component layer (3). The three layers are shown in exploded view disassembled but aligned for assembly.

20

Fluid connection within the system is effected by insertion of ferrules (7, 9) respectively provided at an upper supply aperture in the base board (1) and at an upper outlet aperture in the first level board (2) which are received in the recesses (6, 8) respectively provided in a lower surface of the first level board  
25 (2) and in a lower surface of the second level board (3). In the embodiment, the connection employs simple parallel-sided holes to take PTFE tubes forming the ferrules (7, 9) although it will be understood that more complex holes and ferrules are possible. The ferrules are retained within the holes in interference fit to provide a fluid tight leak proof connection.

In the example shown fluid supply is effected via an inlet fluid source aperture (10) comprising flexible tubing (11) of 1/16 inch (1.5 mm) diameter retained within HPLC fittings (12). The fluid path is shown by the dark line (14).

5 To assemble the modular structure into a laboratory system, a mechanical load is applied in the direction of the arrows (L) to effect engagement between the ferrules (7, 9) and the recesses (6, 8). Additional mechanical fixings (not shown) might be provided to ensure a more secure mechanical connection  
10 between the components (1, 2, 3).

A simple schematic device construction is illustrated in the exploded view in Figure 2. The example device has a sandwich layer structure comprising an external base layer (21) of polyetheretherketone (PEEK), a pair of inner layers  
15 (22) of SU8 epoxy and an upper layer (24) of polymethylmethacrylate (PMMA) and internal layers (22). Channel means (23) are provided in the inner epoxy sandwich layer (22) to provide the necessary microfluidic microstructure. Fluid ports (24) through the upper layer (24) give a fluid communication from a surface of the completed device to the channel means  
20 (23) which form enclosed internal channels once the two parts illustrated in the exploded view of Figure 2 are assembled.

The sandwich layer elements (22) and upper layer (24) contact fluid in use, respectively in the channels (23) and ports (25). Accordingly these are  
25 fabricated from materials exhibiting good chemical resistance, in the example respectively SU8 epoxy and PEEK. Properties of the merely structural lower layer (21) are less critical.

The simple schematic in Figure 2 does not illustrate any active microfluidic devices. It will be understood that these could be incorporated suitably within the channels themselves (for example in particular if these take the form of pumps, valves, filters or the like) or could be incorporated on a module surface in fluid communication with the channels (23).

A microfluidic reaction system in accordance with the invention is illustrated in plan view in Figure 3. The reactor comprises inlets for two supply fluids ("fluid A" and "fluid B"), and provides for three processing streams ("stream 1", "stream 2", "stream 3").

The reactor comprises a baseboard (31) incorporating a plurality of fluid supply channels (32) therewithin. The base board has a number of microfluidic components mounted thereupon, being a manifold (34) to split the supply fluid (A, B) into the three streams (streams 1, 2, 3), and then within each stream a series of modules comprising a mixer chip (35), a detector chip (36), a reactor chip (37) and a further detector chip (36). These components are shown separately in Figures 4 to 8.

A system constructed in accordance with the principles of the invention as illustrated by figure 3 offers admirable simplicity and flexibility, providing a number of advantages over conventional designs. In particular it enables use of larger interconnect components and scaling from the macro to the micro world by microfluidic "fanning" (transition from large pitch to small pitch spacing between fluidic channels). Fittings from chip to board enable close packing of interconnections on  $<2$  mm square packed spacing or  $<1$  mm staggered spacing.



Figure 4 illustrates in plan view the baseboard (31) of Figure 3 without the components attached. The fluid channel means provided within the baseboard (32) are illustrated more clearly.

- 5 The manifold (34) of Figure 3 is illustrated in greater detail in plan view in Figure 5. It can be seen from Figure 5 how the manifold receives from a single inlet the two fluids (fluid A, fluid B) and produces 6 outlets, 1 to 6, effecting a paired supply of fluid A and fluid B to the three streams illustrated in Figure 3.

10

The device is constructed in accordance with the principles of Figure 2. Channel size in the example is 150  $\mu\text{m}$  by 50  $\mu\text{m}$ . Routing is effected through 300 micron channels. The overall size of the device is 62 by 72 by 4 mm.

- 15 Figure 6 illustrates in side view (above) and plan view (below) the micro mixer chip of Figure 3. The micromixer chip receives two fluid streams comprising fluid A and fluid B respectively in inlet A and inlet B. These are mixed together as they follow the flow channel (41) to the outlet. The chip is of a basic design as illustrated in Figure 2, with a channel size of 100  $\mu\text{m}$  by  
20 50 microns and an overall size of 45 by 25 by 4  $\mu\text{m}$ . It is retained in position on the baseboard by means of the clamp (42).

- Figure 7 is a representation of a reactor chip (37) from Figure 3 shown in side view (above) and plan view (below). Fluid flows from inlet to outlet via the  
25 flow channel (51) thereby passing through the reactor portion (53). The reactor portion comprises a catalyst bed (54) 3 mm in diameter and 2 mm deep retained by the screw in plug (55). The overall assembly has a channel size of 100  $\mu\text{m}$  by 50  $\mu\text{m}$ , an overall size of 36 by 25 by 6 mm, and is retained in position by the clamp (52).

Figure 8 illustrates the detector chip (36) of Figure 3 in side view (above) and plan view (below). Fluid flows from inlet to outlet via the flow channel (61). The detector's active area (68) includes a light source in the form of an LED (63) or an optical fibre (not shown) to an external source, a diffraction grating (64) and a light collector in the form of the optical fibre (65). A lens (66) in front of the light source collimates the light and a lens (67) in front of the light collecting fibre improves the light collection efficiency. Collected light is sent for spectral analysis.

10

Additional electrical detection function is provided via groups of 3 gold microelectrodes (69), 110  $\mu\text{m}$  wide on 200  $\mu\text{m}$  pitch. Channel size is 400  $\mu\text{m}$  by 400  $\mu\text{m}$ , giving an overall device dimension of 50 x 30 x 5 mm.

15 It has been noted that systems in accordance with the invention can be given enhanced functionality by using a combination of materials and components and by using composite substrates for the baseboard and chips to achieve the best combination of properties.

20 For example, in the case of a microchemical reactor it is beneficial to use a "window" substrate polymer that is transparent to enable easy inspection of the fluid path, but in which inserts are included in the substrate in the regions where solvent contact is possible; preventing contact with the "window" substrate.

25

An example of such a composite structure is given in figure 9. In the figure different materials are represented by different shading, comprising, in accordance with the illustrated key:

71 - Baseboard substrate material (e.g. PMMA);

- 72 - Chip substrate material (e.g. PMMA)
- 73 - SU-8 epoxy
- 74 - Chemically resistant inserts (e.g. PEEK)
- 75 - Ferrules (e.g. PTFE)
- 5 76 - Fluid connector (e.g. PEEK)

The insert is simply a cylinder traversing the substrate through which is drilled a fluid path way and recess to support a ferrule. The material of the insert can be chosen from high chemical resistance polymers such as PEEK or PTFE or  
 10 in a curable resin formed by micromoulding or lithographically using a photoformable resin. The inserts can be produced by any method including machining or injection moulding.

More complex inserts might have the ferrule integral with the insert. Although  
 15 this would inhibit ferrule replacement it may be a good option for large arrays of chips where multiple ferrule insertion would be time consuming. This is illustrated by the elements 77 in figure 10, where otherwise like numerals are used for like materials.

20 The concept of using a composite approach to achieve the required properties at the optimum location can also be extended to the microfluidic channel walls. The surface properties of the walls should ideally be matched to the desired flow characteristics of the material being transported by the channel. For example, if low wall contact resistance is required a low surface energy  
 25 coating is a more convenient method of achieving the desired effect compared to producing the whole system in a low surface energy polymer. For example, SU8 epoxy treated with Fluorolink S10 (Ausimont)- a di-triethoxysilane based on a linear perfluoropolyether backbone reduces the surface energy to 13

dynes/cm. Conveniently the walls of the channels can alternatively be treated to make them hydrophilic or hydrophobic or to provide biocompatibility etc.

5 A further benefit of the interconnected baseboard and processor chip concept underlying the present invention is the possibility of application to scale up by scale out. Scale out is the term often applied to increasing output from a processor chip performing, for example, a synthetic procedure by multiplying the number of processor chips. This preserves the reaction conditions for the channel dimensions optimised for a single process or series of processes which  
10 would otherwise change if the channel dimensions were increased to achieve higher throughput. This can be achieved by the baseboard functioning as a manifold, supplying reagents to an array of processor chips. The manifold can provide a single sided input to multiple outputs from each processor chip). A manifold on one side can provide an interdigitated input and output array of  
15 channels or one side can provide an input manifold and a higher level board can provide an output manifold.

Examples of such arrangements exploiting the composite concept are shown in figures 11 and 12, respectively illustrating the use of a baseboard as a  
20 manifold for supplying fluid in parallel to an array of processors with multiple outputs from each processor chip and the use of baseboards as input and output manifolds for feeding processor chips in parallel for scale up by scale out or by processor replication. The shading key of Figures 9 and 10 is applied to the systems illustrated in figures 11 and 12.

25

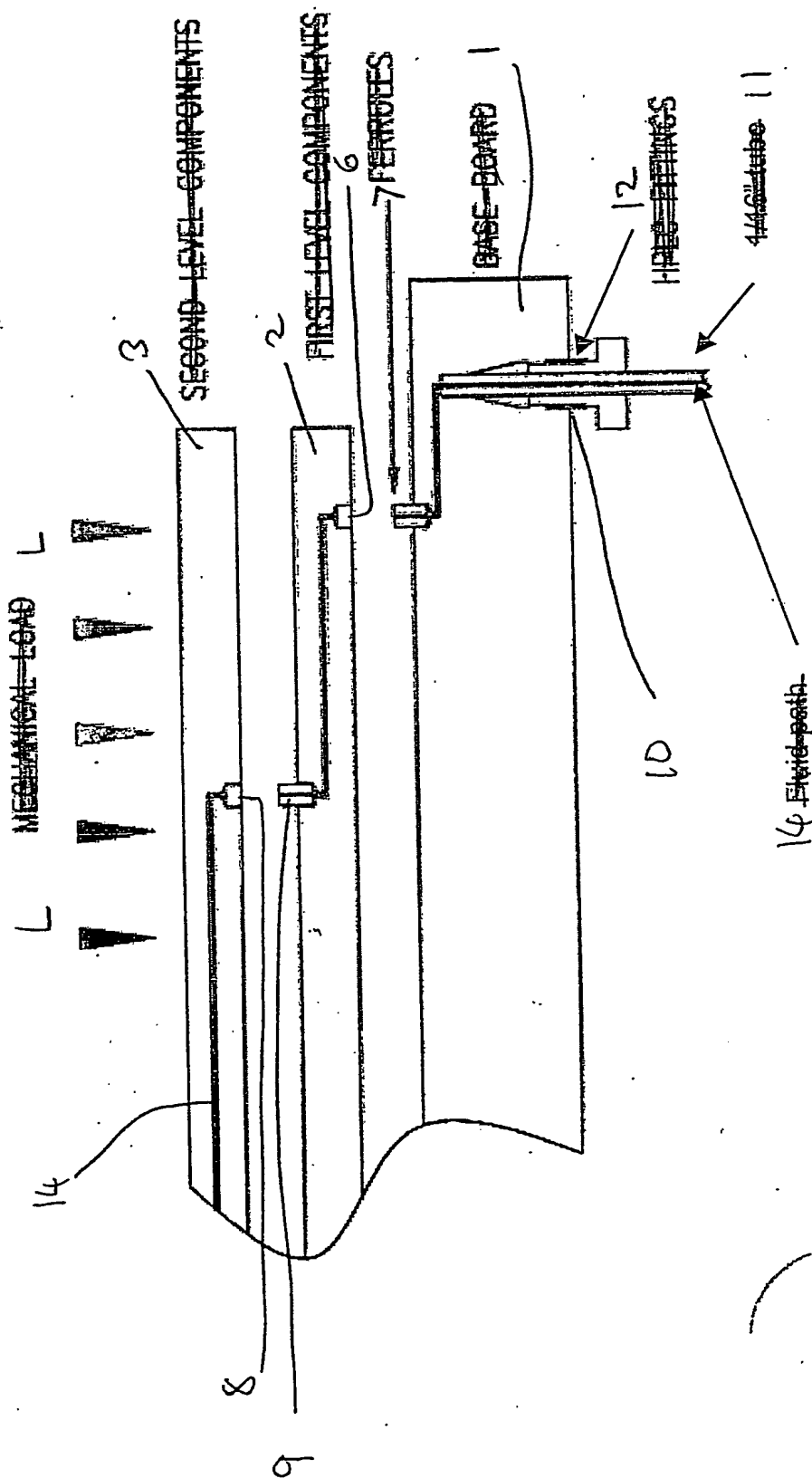
The interconnection system provides a ready means of developing processes by series interconnection of each operation with optimisation of each operation readily achieved by exchange of chips. Once a series of operations are optimised they can be conveniently integrated into a single chip and then if

required converted into arrays with the baseboard providing multiple feeds for use in high throughput screening or the baseboard serving as input and output manifolds for process replication to scale up or achieve increased throughput by scale out. In this way very large numbers of chips can be arrayed to achieve a production capability.

The complete system can be a complete hybrid of materials with for example the baseboard manifold being in polymer, the ferrule seals in polymer, the processor chips in glass, the pumping and valving system in metal possibly with internal polymer seals etc.

1/23/21

# Detail of de-mountable interface

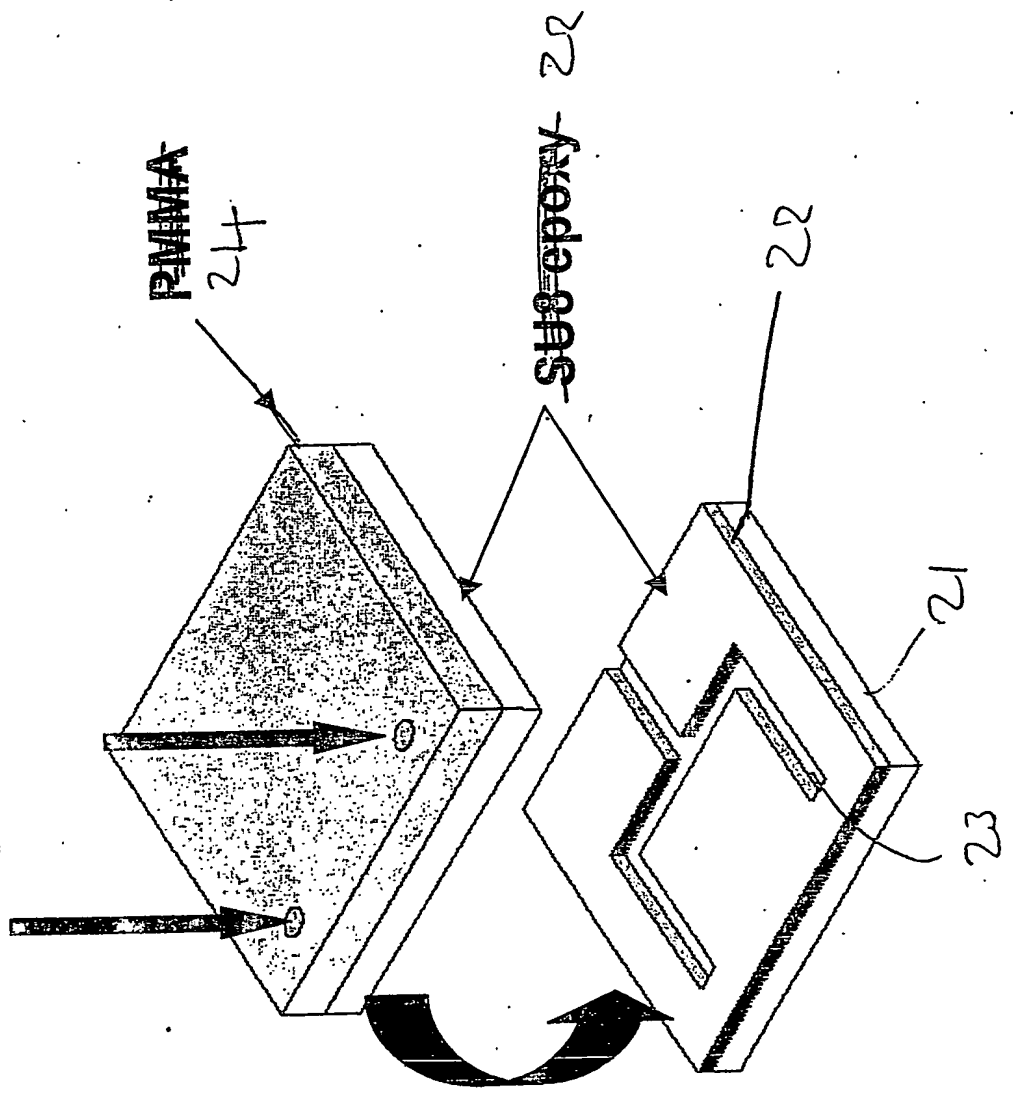


**epigen**

signed

# Device construction

Fluid 25  
ports

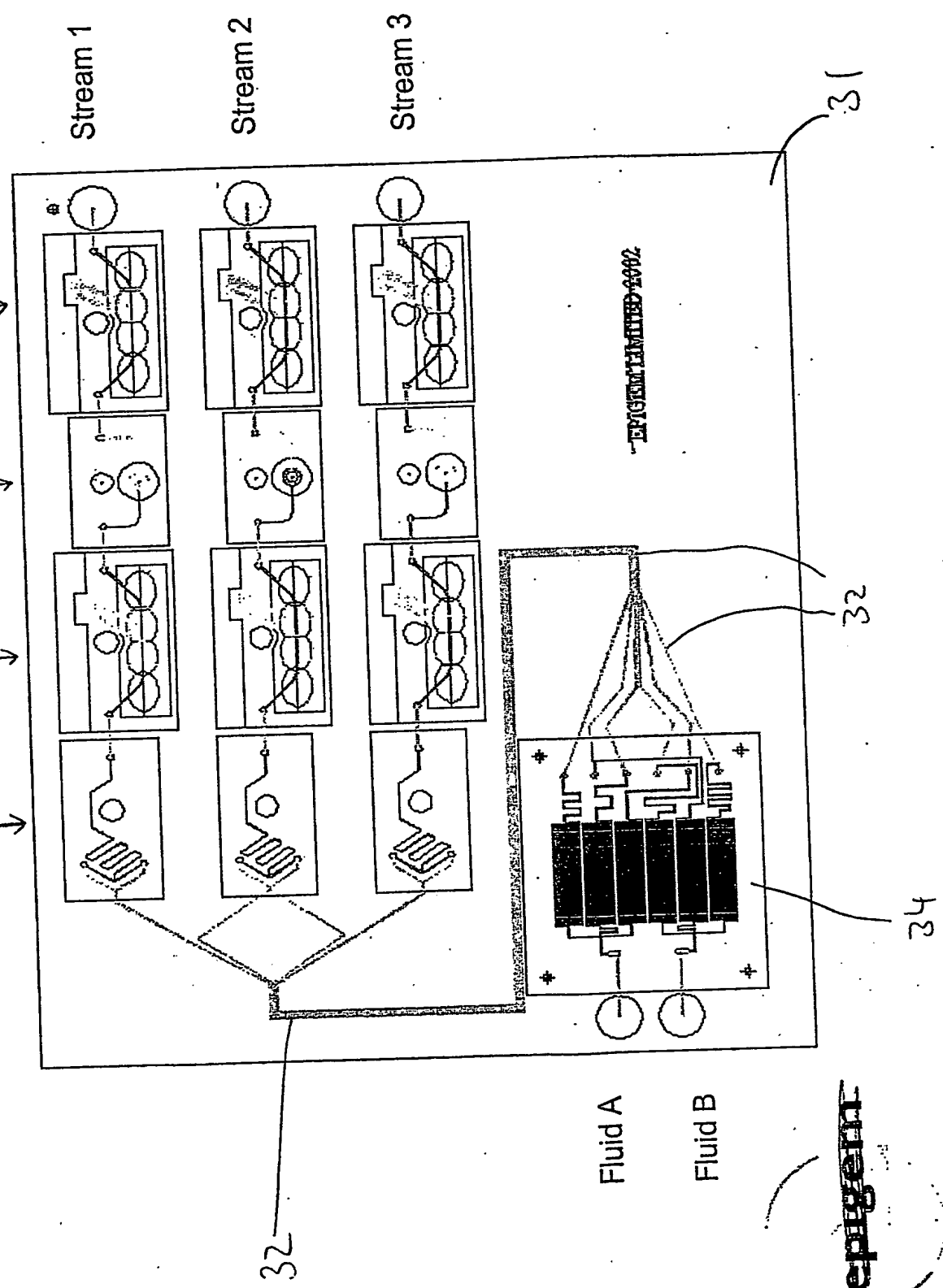


~~Bond~~  
~~on lid~~

epigem

Figure 3

# Microreactor system





1 yw - 1

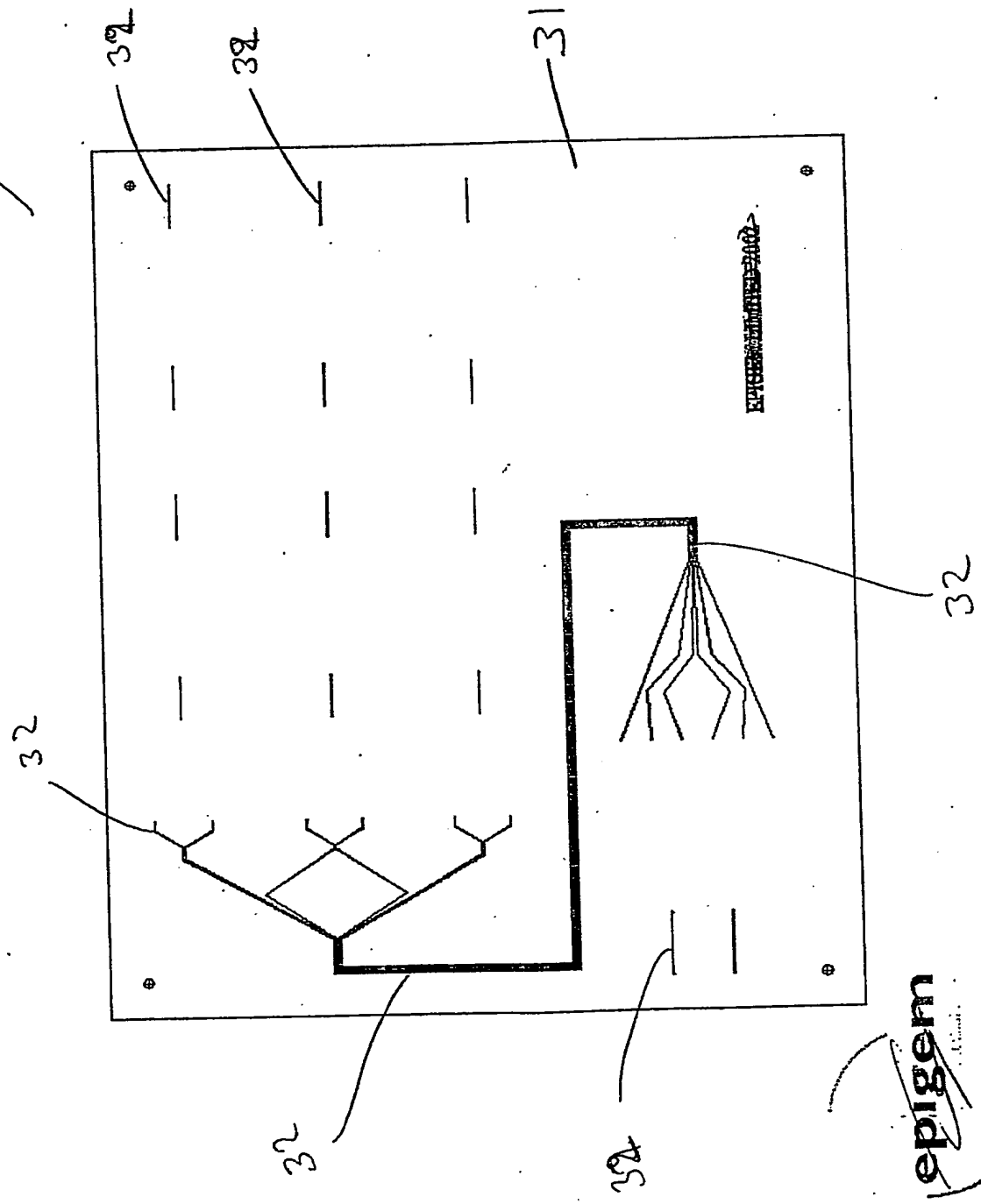
T

# Baseboard

Design

Channel size 200  $\mu\text{m}$  x 50  $\mu\text{m}$

Overall size 250 x 200 x 6-mm



epigern

Figure 5

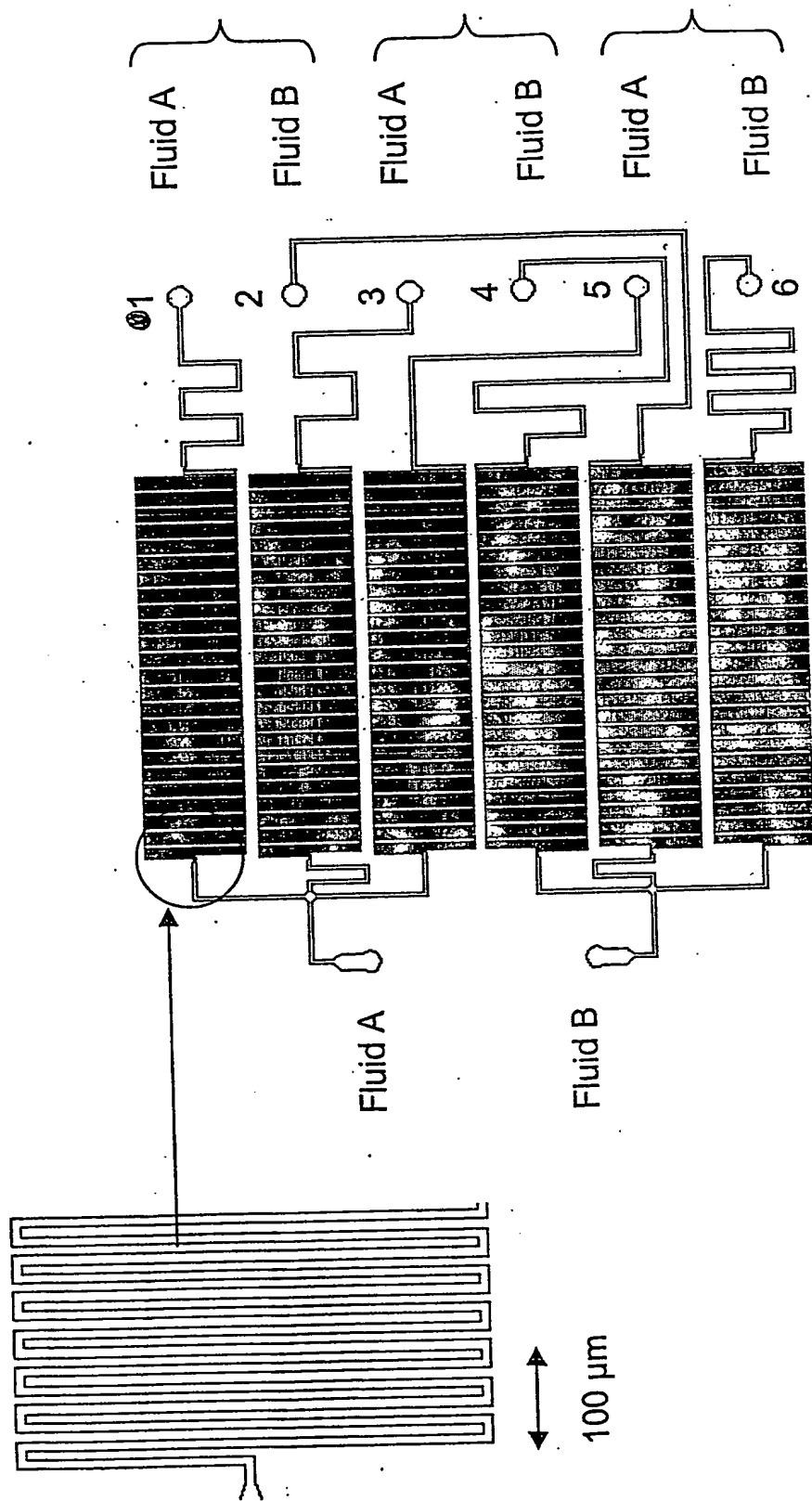
# On-chip manifold

## Design

Channel size  $150\ \mu\text{m} \times 50\ \mu\text{m}$

Routing with  $300\ \mu\text{m}$  channels

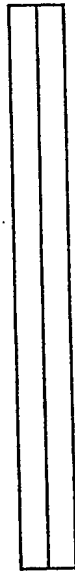
Overall size  $62 \times 72 \times 4\ \text{mm}$



epigem

# Micromixer chip

Side view



Plan view

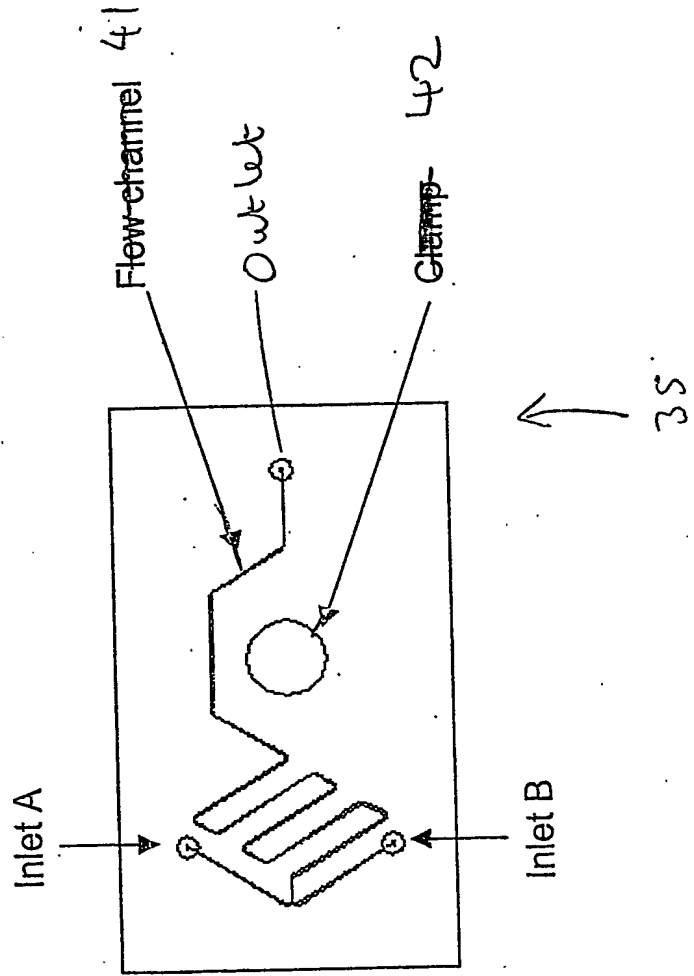


Figure 6

Design

Channel size 100  $\mu\text{m}$  x 50  $\mu\text{m}$

Overall size 45 x 25 x 4 mm

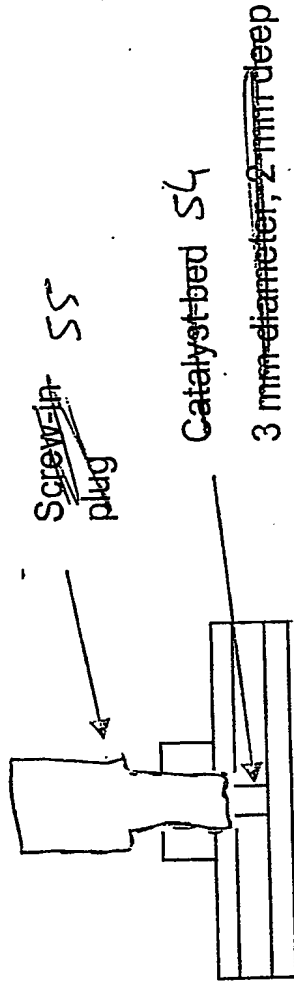
# Reactor chip

Figure 1

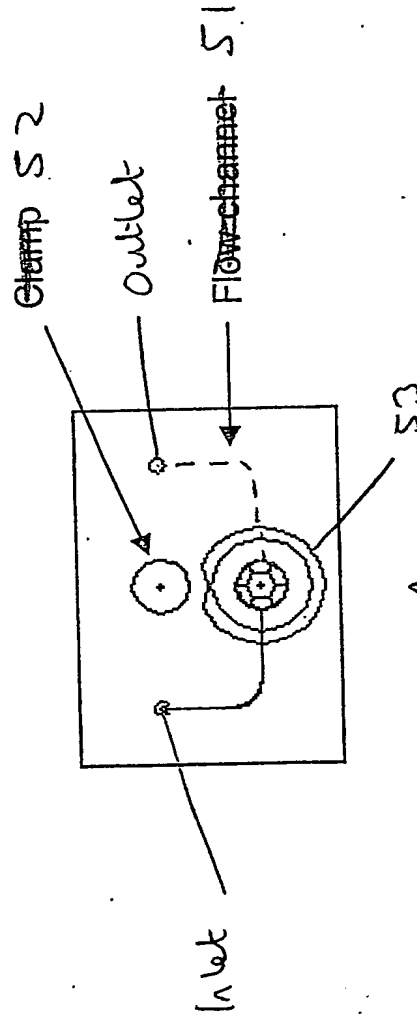
## Design

Channel size  $100\ \mu\text{m} \times 50\ \mu\text{m}$

Overall size  $36 \times 25 \times 6\ \text{mm}$



Side view



Plan view

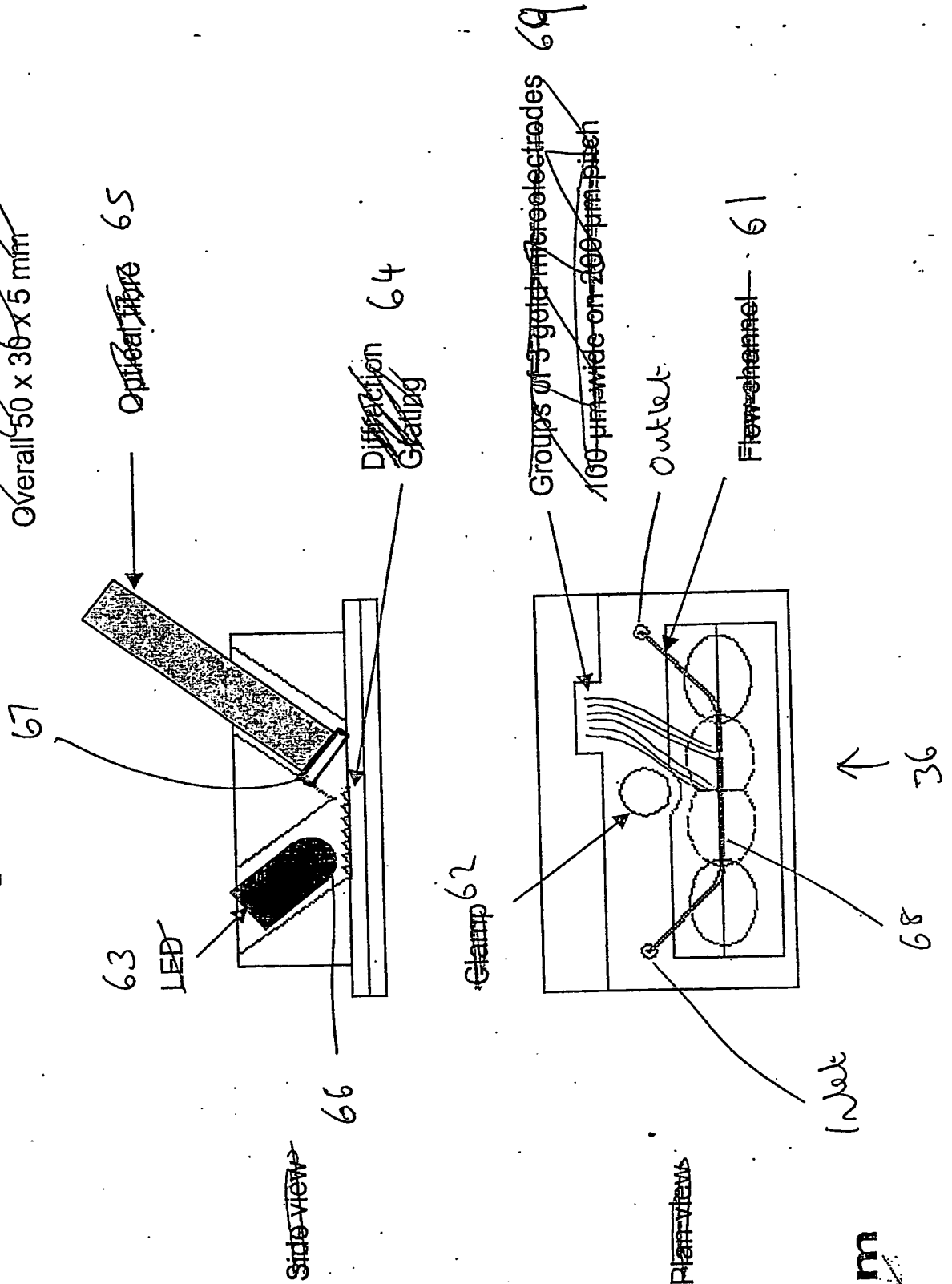
epigen

# Detector chip

Figure 8

## Design

Channel size 400  $\mu\text{m}$  x 400  $\mu\text{m}$   
Overall 50 x 30 x 5 mm



epigem

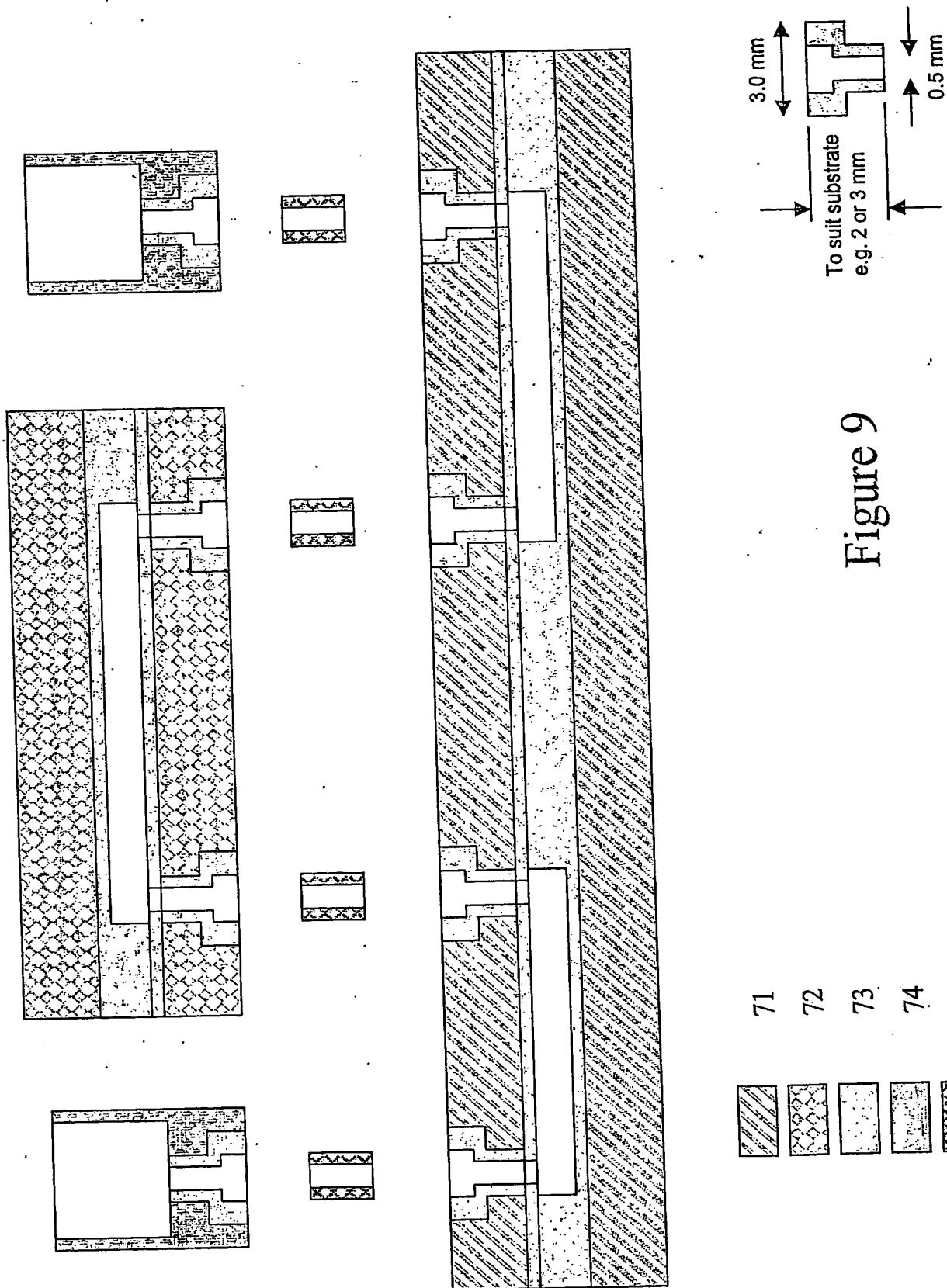
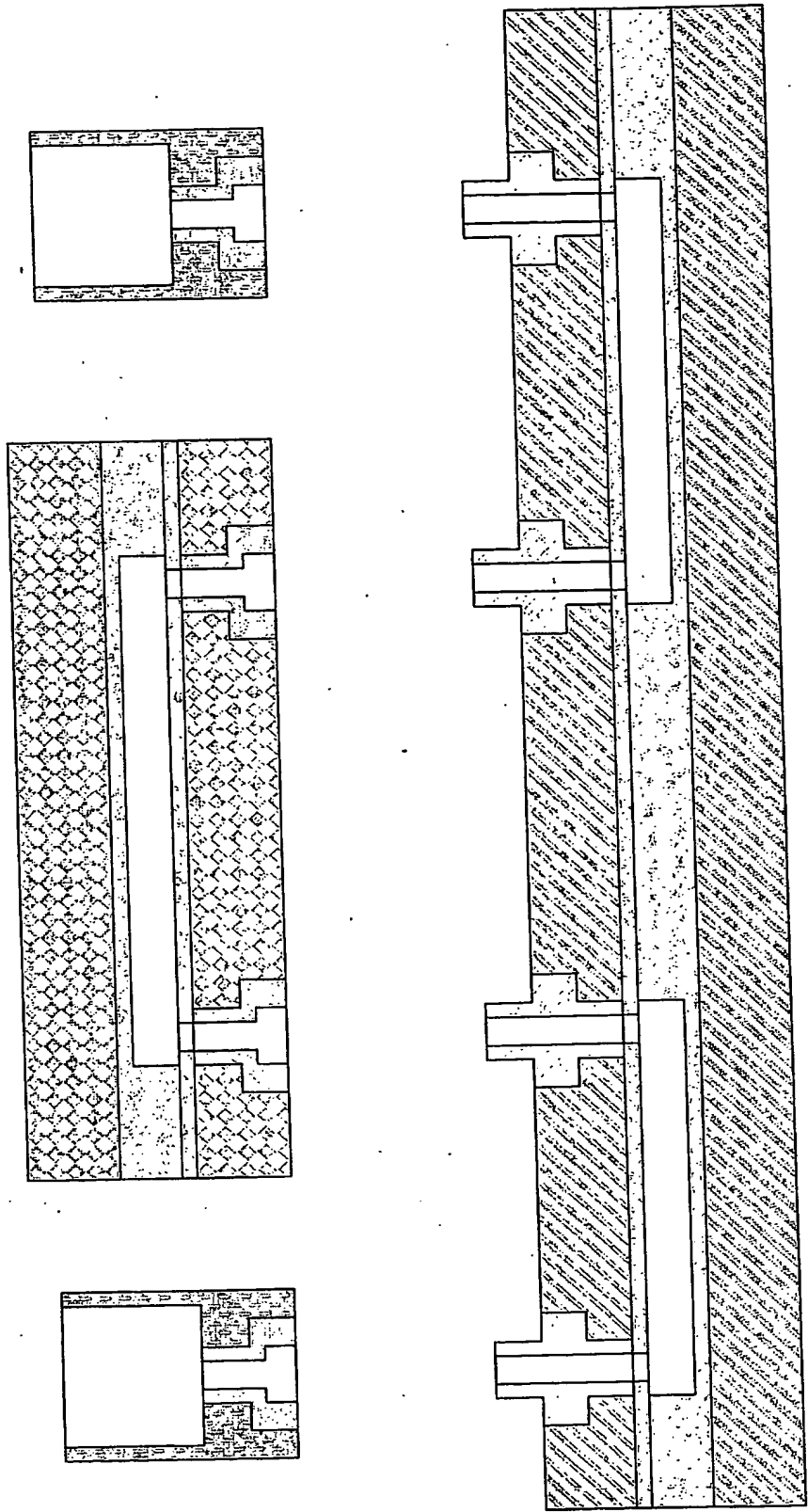


Figure 9



- 71
- 72
- 73
- 74
- 77
- 76

Figure 10

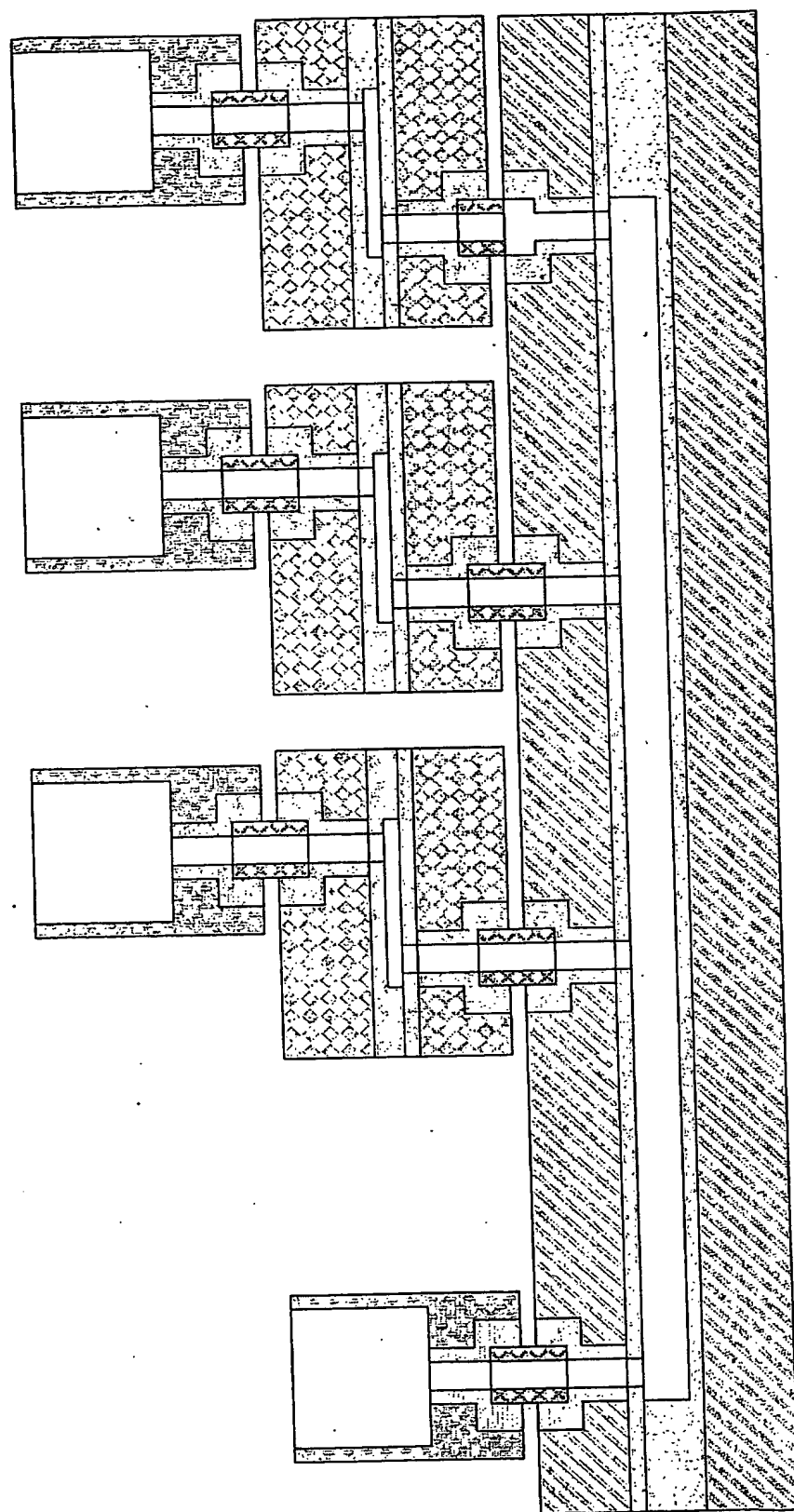


Figure 11



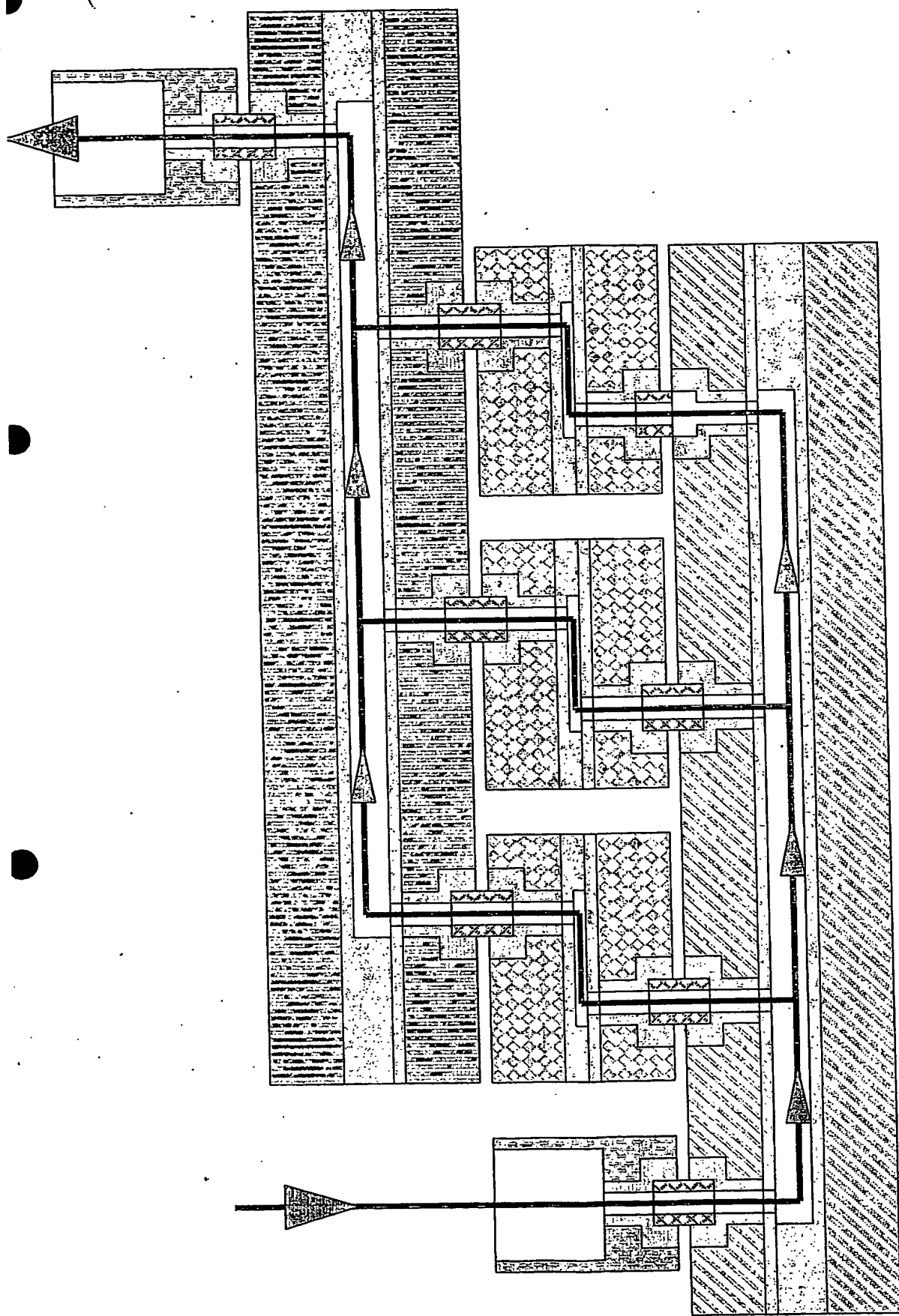


Figure 12

PCT Application

**GB0303853**



**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**